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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,426	08/03/2001	Mark Trulson	3305.1	8231

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EXAMINER

BAKER, MAURIE GARCIA

ART UNIT PAPER NUMBER

1639

DATE MAILED: 04/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE

Office Action Summary

Application No.

09/922,426

Applicant(s)

Trulson et al

Examiner

Maurie G. Baker

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jan 21, 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-79 is/are pending in the application.
- 4a) Of the above, claim(s) 1-55, 57-59, 61-63, and 66-79 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 56, 60, 64, and 65 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e). *See Action.*
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121. *See Action.*

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Applicant's Response filed January 21, 2003 (Paper No. 6) is acknowledged. No claims were amended, added or cancelled. Therefore, claims 1-79 are currently pending.

Election/Restriction

2. Applicant's election of Group XI (claims 56 and 60-65), without traverse, in Paper No. 6 is noted. Claims 1-55, 57-59 and 66-79 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

3. Applicant's election of Species within Subgroup I of nucleotide and Subgroup II of diazonium dye is also noted. Claims 61-63 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected species, there currently being no allowable generic claim.

4. Claims 56, 60, 64 and 65 read on the elected invention and species and are examined on the merits in this action.

Priority

5. Applicant's claim for domestic priority under 35 U.S.C. 120 and 119(e) is acknowledged. However, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date as follows:

The instant application claims priority to case 60/233,290 and also to cases 60/030,826, 09/578,282 and 08/969,227. Most importantly, all of 60/030,826, 09/578,282 and 08/969,227 fail to provide adequate support under 35 U.S.C. 112 for the claims of this application since they do not contain a reference to the step of coating a surface with a photobleachable substance as instantly claimed (e.g. step b)). Only provisional application 60/233,290 discloses such a concept. Moreover, the relationship of cases 60/030,826, 09/578,282 and 08/969,227 to the instant application is unclear. Thus, instant claims are only awarded the date of provisional application 60/233,290, which is August 3, 2000.

Claim Objections

6. Claims 60, 64 and 65 are objected to because of the following informalities:

The multiply dependent claims depend from non-elected claim 57, which is improper. Amendment of the claims to depend from only elected claim 56 is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 56, 60, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to a "method for synthesizing a polymer array". There are a virtually unlimited number of compounds that would fall within the claimed genus of "polymer array". Moreover, the claims go on to recite that a "photobleachable compound or group" is used. There are a wide variety of compounds that would fall within this genus as well. The instant specification discloses only very limited examples carrying out the claimed method. This disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus.

Note that the language of the specification should describe the claimed invention so that one skilled in the art can recognize what is claimed. A description of a compound in terms of its function fails to distinguish the compound from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *University of California v. Eli Lilly*

and Co. (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398

7/22/1997 Decided July 22, 1997; No. 96-1175).

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (cited above) regarding disclosure. For adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by “representative examples”) for both enablement and adequate disclosure.

9. Claims 56, 60, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for creation of polynucleotide or polypeptide arrays using pyrylium or diazonium dyes as the photobleachable compound, does not reasonably provide enablement for making **any** “polymer array” using **any** “photobleachable compound or group”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is clear from applicant’s specification how one might practice this invention for making polynucleotide or polypeptide arrays using pyrylium or

diazonium dyes as the photobleachable compound; however, there is insufficient guidance as to how to make/use **any** “polymer array” using **any** “photobleachable compound or group”. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors can include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to “method for synthesizing a polymer array” that utilizes a “photobleachable compound or group”. Both “polymer array” and “photobleachable compound or group” could read on a wide variety of structures. Such represents broad scope.

(3 and 5) The state of the prior art and the level of predictability in the art:

Various arrays and photobleachable compounds were known in the art at the time of filing; however, only limited numbers of such entities were known and the specification gives no guidance to permit one of skill in the art to devise strategies for the making of *any* “polymer array” and the use of *any* “photobleachable compound or group”. The structures of possible variants are sufficiently diverse and one of ordinary skill would not be able to predict their structures. Polymers

of various structures would require completely different chemistries. The use of different photobleachable compounds or groups would also require differences in preparation and use. One of ordinary skill could not guess, *a priori*, how to make and use **any** such “polymer array[s]” and “photobleachable compound[s] or group[s]” as one could not necessarily predict the required chemistry in the absence of any guidance without undue experimentation. Applicant’s claimed scope represents only an invitation to experiment regarding possible “polymer array[s]” and “photobleachable compound[s] or group[s]” of undefined structure.

(4) The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have provided only very limited examples of the claimed methodology. No generic strategy for determining the required chemistry for making *any* “polymer array” and using *any* “photobleachable compound or group” is provided. Specifically, the instant specification fails to identify that structure which is required for the claimed activity. The teachings of the instant specification coupled with the examples only support making polynucleotide or polypeptide arrays using pyrylium or diazonium dyes as the photobleachable compound. See also written description rejection above.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: The instant specification does not provide to one skilled in the art a reasonable amount of guidance with respect to the direction in which the experimentation should proceed in carrying out the full scope of the claimed method. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir. 1991). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure, one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 56, 60, 64 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- A. Claim 56 (and claims dependent thereon) recites in step a) the term “synthesis groups”. This lacks clear antecedent basis as the claim refers earlier to “synthesis intermediates”.
- B. Claim 56 also recites in step b) “photobleachable compound or group” (emphasis added), but then goes on to recite in step c) “said photobleachable compound”. Thus the phrase also lacks clear antecedent basis.
- C. Also, the objective of the method is unclear. Claim 56 recites a “method for synthesizing a polymer array”. However, a polymer array is not formed by the instant method. In the last step (i.e. step; g)) a “desired polymer sequence is obtained”. This creates confusion and thus the claim is indefinite.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not

commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 56, 60, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pirrung et al (US 5,143,854), in view of Zebala (US 6,159,681).

Pirrung et al teaches synthesis of polypeptide arrays using photoremovable protecting groups (see Abstract, column 3, Figures 1-7 & 14A). As shown in the reference, polypeptides are built up on a substrate using amino acids with photoremovable protecting groups such as NVOC which reads on the claimed “synthesis intermediates” and “photosensitive protecting groups”. The protecting groups are selectively removed by irradiation through a mask; this is performed to create a desired sequence. See, for example, column 28, lines 12-66 of Pirrung et al, which teaches the monomer-by-monomer synthesis of the sequence YGGFL. Pirrung et al teaches that nucleotides can also be used as monomers in their method (see, column 6, lines 9-21, especially line 14), reading on the instant claim 50. The reference also teaches that contrast enhancement materials can be applied between the mask and the substrate to “enhance contrast of light applied to the substrate” (see column 14, lines 5-16). These materials comprise molecules that are “transiently bleached at the wavelength of interest”, which allows “greater penetration where light is applied, thereby enhancing contrast” (see column 14,

lines 10-16). Molecules such as “quinone diazid” are taught, reading on the instant claims 54 and 55.

Thus, although Pirrung et al does teach the use of a contrast enhancement layer (as described in the instant specification, page 19, lines 15-23), Pirrung lacks the specific teaching of *coating the surface having the synthesis intermediates thereon* with a substance comprising a photobleachable compound or group (i.e. instant step b)).

However, using coatings directly on the molecules of interest was well established in the art at the time of filing as taught by Zebala. The reference teachings using a “photoresist layer that is established over a biologic material (which may be immobilized on a substrate). Regions of interest are selected and irradiated to expose specific regions of biologic material” (see Abstract). The biologic materials of Zebala can be peptides or nucleotides (see column 8, lines 46-56). Coating of the photoresist on the biological material is taught, for example, in column 8, line 57 – column 9, line 16 and photoresists are discussed in columns 14-15 of the reference. The reference teaches that using the photoresist directly on the biologic material facilitates analysis of discrete regions (see, e.g. column 6, lines 40-65). Zebala also teaches that contrast enhancement materials can be applied between the mask and the substrate to “enhance contrast of light applied to the photoresist” (see column 31, lines 23-35). These materials comprise molecules that are “transiently bleached by light”, which allows “greater

penetration where light is applied, thereby enhancing contrast” (see column 31, lines 25-29).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing to carry out Pirrung’s synthesis of polypeptide (or polynucleotide) arrays using photoremovable protecting groups further utilizing a photobleachable layer directly coated on the array as taught by Zebala. One would have been motivated to do so due to the advantageous properties of such photobleachable layers (i.e. contrast enhancement materials) as taught by both references, e.g. allowing “greater penetration where light is applied, thereby enhancing contrast”. One would have been motivated to place such a layer directly on the materials of interest since such facilitates analysis of discrete regions as taught by Zebala.


Status of Claims/Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant’s disclosure.
 1. Gao et al (US 6,426,184): Method and apparatus for performing chemical and biochemical reactions in solution using in situ generated photo-products as reagent or co-reagent. See Abstract.
 2. WO 98/20967: Radiation directed combinatorial synthesis of arrays using radiation-activated catalyst, autocatalytic reactions and protective groups. See Abstract.
16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
March 31, 2003



MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER